

Opioid Substitution and Pregnancy

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Methadone in pregnancy

- ▶ Many misconceptions, and much resistance to use
 - Patients worry about it in pregnancy
- ▶ Uninformed healthcare providers (HCPs) see methadone as a marker of high risk and potential parenting issues/poor judgement/etc
 - I see it as evidence of ongoing engagement in care and sign of opportunity for great change

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Objectives

- ▶ Consider rationale for opioid substitution in pregnancy
- ▶ Discuss pregnancy/neonatal issues
- ▶ Investigate the issues regarding methadone in antenatal and peripartum care

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Patient experiences

- ▶ Government Accountability Office report (US – 2014)
 - “Viewing pregnant patients with opioid use disorders as criminals or de facto child abusers is currently a real barrier to care and most likely to healthy pregnancies”
- ▶ 2014 – Tennessee law specifically targets opioid dependant pregnant women for prosecution for fetal assault

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Opioid use in pregnancy

- ▶ Not a heterogeneous group of people
 - Some actively using illegally acquired drugs
 - Some on prescribed opioids
 - Some on methadone/buprenorphine
- ▶ Each situation confers different risk to mother/fetus
 - Peak/troughs, episodes of withdrawal, NAS implications

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Study on physician attitudes

- ▶ Survey of women (n=26) who had encountered physician prior to starting their methadone therapy
 - 88% told the physician of their pregnancy and opioid use
 - 57% found the physician helpful/supportive
 - 43% found them unhelpful
 - 10 were referred to a methadone program
 - One patient talked to 3 different physicians and never did get a referral to help

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Study on attitudes

- ▶ Patients:
 - My baby will be “retarded”, “disabled with violent outbursts”, born with “brain damage” or “heart failure”, or “not breathing and need a shot to breathe”
 - Physicians exacerbated the brain damage fears
 - Some patients on chronic opioids for pain told immediately stop
 - One had her methadone dropped from 100 to 40 mg/d
 - Two patients told that a withdrawal precipitated miscarriage would be the best outcome

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Methadone in pregnancy

- ▶ Methadone facilitates antenatal care
 - Longer pregnancies, fewer complications
 - Infants who are larger for their gestational age
- ▶ Protects her fetus from:
 - Peaks and troughs of drug levels
 - Illicit drugs of unknown composition
 - Injection-related viral infections

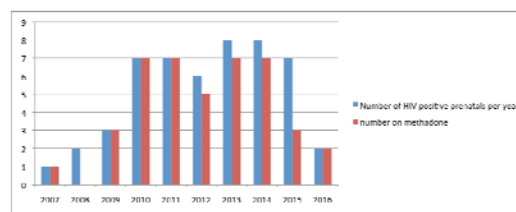
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Why to use methadone in pregnancy

- ▶ Stop the chaos and establish normalcy in day to day life.
 - Time spent on accessing drugs, chaotic relationships, legal issues
 - Can't deal with necessities of life – housing, food, the basics, etc – “determinants of health”
 - Chaos slows down, can deal with other issues
 - Counselling, relationships, prenatal care, nutrition, education

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Why use methadone in pregnancy

- ▶ Engagement with addictions/detox and other care.
 - Linkage with daily methadone therapy – IE: ARVs
 - Linkage of PN care visits with methadone visits
- ▶ Decreased transmission of HIV, Hep C and other blood born infections; endocarditis
 - Safe in pregnancy, and much MUCH safer than ongoing use

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Methadone in pregnancy

- ▶ Withdrawal and risk to fetal brain
 - An untreated mother puts the fetus at great risk
 - Maternal withdrawal: catecholamine surge, uterine contractions, reduced placental blood flow and O₂ transfer
 - Fetal withdrawal: Increased motor activity, increased O₂ demands, rises in norepinephrine levels in AF
 - Together, this can precipitate preterm labour, fetal hypoxia, and fetal demise
 - Rate of relapse is very high

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Withdrawal and the fetal brain

- ▶ Stress related programming and the fetal brain
 - Permanent changes occur due to stress levels
 - Prolonged surge in corticosteroids
 - Signals poor maternal condition to fetus
 - Rapid modification of neurotransmitter systems and transcriptional machinery
 - Permanent modification in behaviour/brain morphology/neuroendocrine function
 - Epigenetic modifications that may be heritable, predispose to stress related disease in later life
- Our monitoring only picks up life threatening stress
 - most of this is not detectable

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Split dosing

- ▶ Split dosing may help
 - Half life in T3 mothers may be half that of non-pregnant populations
 - At least BID dosing helpful, or greater (QID)
 - Important that methadone dose meets need to reduce relapse and chronic met/fetal stresses
 - Rapid reduction to normal metabolism postpartum
 - Careful monitoring especially if breastfeeding

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Fetal stress

- ▶ Considerable emotional stress for women with opioid dependence, and often co-existing anxiety disorders
 - Anxiety and stress alone increase preterm delivery and low birthweight
 - Increased SA, reduced HC, lower neurologic scores, increased crying, difficulty soothing and evidence of long term functional disorders assoc with maternal stress
- Studies do not really account for this major confounder of infant outcomes

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Buprenorphine vs methadone

- ▶ Meta-analysis (2015)
 - 3 RCTs, 15 cohort studies (n= 223, 1923 respectively)
 - Compared to methadone
 - Lower risk PTB (RR=0.67)
 - Greater BW (~256 g)
 - Larger head circumference
 - No change in perinatal death/congenital anomalies
 - One study suggests, but almost all in unsafe sleeping arrangements, mother heavy smoker

Addiction (2016) 111, 2115-2128 (Zedler et al)

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Methadone dosing in pregnancy

- ▶ Significant pharmacokinetic changes occurring pregnancy
 - Increase blood volume by 50% - increased volume distribution
 - Slowed gastric emptying and longer GI transit times - may enhance absorption
 - Body fat changes affect accumulation
 - Increased hepatic methadone metabolism due to increased CYP enzymes
- ▶ Adjustments made on clinical s/sx

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Can Jour Hosp Pharmacy (2012), 65(5)

Buprenorphine vs Methadone

- ▶ Similar NAS outcomes
- ▶ Duration of NAS
- ▶ Infant hospital stay
- ▶ GA at delivery
- ▶ Summary - Buprenorphine should be considered at least an equivalent option to methadone

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Ann of Pharmacology 2016, 50(8) 666-672 (Noormohammadi et al)

Neonatal abstinence syndrome

- ▶ Clinical Diagnosis
 - Consequence of abrupt discontinuation
 - CNS predominant symptoms, GI
 - May be severe and intense
 - Rarely fatal but prolonged hospital stays
 - Short acting opioids cause more severe and protracted NAS
 - Increasing in diagnosis
 - 3.4/1000 LB (Florida) – much higher here
 - Often confounded by PTB, IUGR, LBW

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NAS

- ▶ Studies have suggested that hospital response dictates expression of NAS
 - NICU admission increases rates of medication need for NAS treatment
- ▶ Hospital handling of NAS more impact on NAS expression than the dose of methadone!

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NAS

- ▶ Good evidence that higher dose of methadone does not cause worsened NAS
 - Divided dosing is most physiologic for the fetus, and minimizes fetal stress
- ▶ Most importantly – opioid use does not preclude good mothering

Addiction 2010, Neurotoxicol Teratol 2013

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Effects of MMT on antenatal testing

- ▶ At peak levels – FHR is slower with less variability and accelerations
 - Longer NSTs, less “reactive”
 - Much longer BPPs (4 min vs 19.8), but score same
 - Less fetal activity may be noted
 - Split dosing seems to have less effect on FHR
 - Seems to be less effect on FHR from buprenorphine

Clin Obstetrics and Gynecology 2013, 56(1), 154-165 (Koppel et al)

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NAS

- EXTREMELY important to keep mother and baby together as much as possible
 - Control of environment minimizes neonatal stress
 - Babies need their mothers
 - Increased heart rate, reduces sleep and increased NAS scores if removed from their mothers for “observation”
 - Separation decreases maternal attachment and increases risk of neonatal abandonment
 - Rooming in promotes more effective “mothering” and reduces prevalence and severity of NAS
 - Long term contribution to outcome??

JOCC 2016, AJOG Mar 2017

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Effect of MMT on pain control

- ▶ Methadone should be continued until caesarean/delivery and postpartum/post-op
 - Acute pain should be treated – opioids and non-opioids
 - Neuraxial/regional techniques for pain control when possible
 - If not on oral meds – may continue IV meth in hospital
 - Buprenorphine
 - Stop 72 hrs pre-op (or convert to meth)
 - May use opioids then as indicated

Curr Pain Headache Rep (2016) 20:16, (Sen et al)

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